IN THE ABSTRACT:

Please insert new page 30 attached hereto as the "ABSTRACT".

REMARKS

Entry of the foregoing, and reexamination and reconsideration of the above-identified application are respectfully requested.

The specification has been amended to insert a "Cross Reference to Related Applications", to insert several headings into the application, and to add an Abstract as required by the rules. The claims have been amended to clarify the language of the claims. In addition, claim 29 was amended without prejudice or disclaimer of the subject matter to delete reference to a non-elected invention.

In the Official Action, Applicant's election with traverse of Group I, claims 17-19, 22, 24, 26, 28, 29, 30, 31, 33, 35 and 37 (16-18, 21, 23, 25, 27, 28, 29, 30, 32, 34 and 36), was acknowledged. The Official Action states:

> The traversal is on the ground(s) that, no arguments were presented. This is not found persuasive because the inventions as claimed are independent and distinct and define patently different inventions. The requirement is still deemed proper and is therefore made FINAL.

This statement is not understood. The traversal of the restriction requirement was not on the grounds that no argument was presented. Instead, the traversal was on the grounds that technical features form a special technical relationship among the inventions of the present application, and that the technical feature is the *T. equigenitalis* specific monoclonal

antibodies of the claims of Group I. In view of this technical feature, unity of invention was said to exist in view of MPEP §1893.03(d). *See,* Response to Restriction Requirement and Preliminary Amendment dated December 9, 1999.

More specifically, the simple fact that an antibody does not recognize the same epitope as another antibody, or is obtained through the use of a different antigen is in itself not a proper ground for lack of unity of invention under PCT Rule 13, which should be applied to the instant application since it is a US national phase application. Reconsideration of the requirement for restriction under PCT Rule 13 and MPEP Chapter 1800 is respectfully requested.

An explanation of the statement in the Official Action and reconsideration of the Restriction Requirement in light of applicants' actual arguments are thus respectfully requested.

The Official Action notes that the specification should refer to the priority documents upon which the instant application is based. The specification has been amended accordingly.

With respect to the drawings, applicants note that formal drawings have been filed at WIPO, as requested by the PCT. These formal drawings should be received by the U.S. Patent Office.

Various informalities of the application were noted in paragraph numbers 10-13 of the Official Action. These informalities have been corrected by the instant amendment.

With respect to the abbreviation "ED" at page 20, this is now defined at page 17 of the application.

Regarding the renumbering of the claims, it is noted that applicants numbered the claims in the Preliminary Amendment based upon the most recent amended claims in the PCT application. As shown in the translation of the amended claims of International Application No. PCT/FR97/00649 as filed on April 11, 1997, the claims were amended to include claims 1-15, rather than claims 1-16 as originally filed in the PCT. These claims as amended were the claims which entered the national phase in the U.S. Therefore, applicants' designation of claim 16 as the next newly added claim in the Preliminary Amendment dated October 9, 1998, is believed to be correct. The claims should not have been renumbered as done at page 2 of the Official Action. It is respectfully requested that the numbering of the claims be returned to that originally presented by applicants.

Claim 24 (23) has been rejected under 35 U.S.C. §112, first paragraph, as allegedly not being enabled by the specification. This rejection is respectfully traversed.

The invention of claim 23 is fully enabled by the specification. At the very least, methods for obtaining a hybridoma according to claim 23 are given in the specification, for example, at pages 4-5 and in Example 1. By following the experimental procedure described in example 1, for example, a person skilled in the art would obtain a bank of hybridomas according to claim 23, fourteen of them are described in further details, their specificity being checked in example 2. Moreover, particular epitopes were isolated and described in the application. *See, for example,* claim 17, and Example I, particularly page

19. Particular epitopes can also be easily identified with a monoclonal antibody of the invention (*see, e.g.,* page 6 lines 24-30).

Furthermore, a hybridoma cell line has been deposited under the terms of the Budapest treaty at the CNCM (Institut Pasteur, France). Three deposit declarations (signed by the two inventors, and by the representative of the assignee), together with a copy of the CNCM deposit receipt are submitted herewith.

Withdrawal of this rejection is respectfully requested and believed to be in order.

Claims 17-19, 22, 24, 26-31 and 33-36 (16-18, 21, 23, 25-30) have been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which is not described in the application. This rejection is respectfully traversed.

According to the Official Action, no specific epitopes or conformational structure(s) which define epitopes have been described. The Examiner states that there is no written description of specific epitopes of a bacterium whose genus is different from *Taylorella* or epitopes of *Taylorella* species which differs from *equigenitalis*; such species have allegedly not been described by their amino acid sequence or carbohydrate bonds so as to define the antigenic structures. This assertion is in error. As stated *supra*, the description in Example 1 of the application enables a person skilled in the art to obtain a wide range of hybridomas of the invention (*see,* Deposit Declarations submitted herewith). Particular epitopes which were isolated in accordance with the teachings of the application are described, for example, in Example I, particularly page 19. Following the teachings of the application,

additional epitopes could be easily identified by a person skilled in the art using a monoclonal antibody of the invention (*see, e.g.,* page 6 lines 24-30).

Withdrawal of this rejection is respectfully requested and believed to be in order.

Claims 18, 19, 22, 26, 27, 30, 31 and 35 (17, 18, 21, 25, 26, 29, 30 and 34) have been rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. This rejection is traversed in part and rendered moot in part.

Claims 16-18 have been amended to recite "isolated and purified" to overcome this rejection. Claim 17 has been amended as helpfully suggested by the Examiner to specify "Fv, Fab and F(ab')2 fragments." With respect to the specificity of the antibodies of claim 17, it is noted that this claim depends on claim 16. Through this dependency, the antibodies of claim 17 must recognize "an epitope of a bacterium of the species *T. equigenitalis*." Claim 17 is thus believed to be sufficiently definite to a person skilled in the art. Claim 18 has been amended as helpfully suggested by the Examiner to recite "hybridomas" instead of "hybrids."

Clarification of the phrase "by means of an inactivated strain" was requested. Since this language has been deleted from the claim, clarification is not necessary. Claim 18 has also been amended to clarify that it is the monoclonal antibody in the supernatant, and not the supernatant, which specifically binds to epitopes.

Claim 22 (21) was rejected on the basis that the meaning of the phrase "by means of a strain of the species T. equigenitalis or extract(s) from such a strain" is not clear. This

claim has also been amended to delete the language noted in the rejection in order to clarify the meaning of the claim.

Claims 26 and 31 (25 and 30) are said to be indefinite because the upper limit of "at least one monoclonal" is not recited. An upper limit is not required to be recited in the claims. Under 35 U.S.C. §112, second paragraph, a specification shall include claims "particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." Determining whether a claim is indefinite requires an analysis of "whether one skilled in the art would understand the bounds of the claim when read in light of the specification.... If the claims read in light of the specification reasonably apprize those skilled in the art of the scope of the invention, [section] 112 demands no more." *Credle v. Bond*, 30 U.S.P.Q.2d 1911, 1919 (Fed. Cir. 1994). One skilled in the art could readily determine what an upper limit should be. One skilled in the art would recognize based upon the teachings of the application that more than one monoclonal antibody could be contacted with the specimen or culture to be analyzed in order to permit a reaction of the antigen-antibody type. One skilled in the art could determine, without undue experimentation, whether a particular quantity of monoclonal antibodies would work in the method of the claims.

In claim 27, clarification of the phrase "one or more monoclonal antibodies" is requested. Again, as stated above, no upper limit is necessary in the claim and the phrase "one or more monoclonal antibodies" would be sufficiently definite to a person skilled in the art.

In claim 25, the Examiner requests clarification of the antigen and epitopes participating in the reaction and asserts that the claim recites "any product formed." Please note that claim 25 does not recite "any product formed," but instead specifies "any product formed in a reaction of the antigen-antibody type." This clearly excludes non-specific product not indicative of bacterial infection, and product formed by reactions due to agglutination and precipitation of the antibodies. Because claim 25 relates to the detection of antigen-antibody reactions due to antibodies which have the specificity defined in claim 16, the detection necessarily has the required specificity. Claim 25 thus distinctly claims the invention.

Claim 29 is said to recite non-elected subject matter and has been amended to recite only the elected subject matter.

Claim 34 is said to be indefinite in view of the recitation of "blocked by saturation of the specimen obtained by means of a serum from which anti-*T. Equigenitalis* antibodies have been removed." This claim has been amended to recite that the non antigen-antibody reaction is "blocked by saturation of the collected specimen through incubation with a serum which does not contain anti-*T. equigenitalis* antibodies". This language is believed to be sufficiently clear to a person skilled in the art.

In view of the above, withdrawal of the rejection of the claims under §112(2) is respectfully requested and believed to be in order.

Claims 17, 19, 22, 24, 26 and 28 (16, 18, 21, 23, 25 and 27) have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Friedrich (1995). This rejection is respectfully traversed.

According to the Official Action, Friedrich inherently discloses monoclonal antibodies produced by hybridomas as claimed by applicants. This assertion is in error. Friedrich (1995) mentions that anti-*T. equigenitalis* monoclonal antibodies have been used for examination of infected organs. The disclosure is, however, limited to this mention. No additional information is provided. For example, there is no description of the technical features of these monoclonal antibodies, and no indication regarding how to obtain them. Nor does Friedrich (1995) mention or even suggest that these monoclonal antibodies have any kind of specificity. There thus is nothing in Friedrich (1995) to even suggest that the monoclonal antibodies have the particular specificity of those claimed by applicants. The Federal Circuit has previously held that prior art is anticipatory only if every element of the claimed invention is disclosed in a single item of prior art in the form literally defined in the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 231 USPQ 81, 90 (Fed. Cir. 1986), *cert denied*, 480 US 947 (1987). This standard is clearly not met by Friedrich (1995).

Withdrawal of this rejection is respectfully requested and believed to be in order.

Claims 17, 18, 19, 22 and 24 (16, 17, 18, 21 and 23) have been rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Akuzawa et al (1996). This rejection is respectfully traversed.

The document cited in the Official Action is in Japanese and no translation was provided. The rejection was based solely on the title and of the appearance of the words "Mab NA-1", "NA-2" and then "28-44 kDa" among Japanese characters. Based upon only the appearance of these three phrases, it is asserted that Akuzawa (1996) discloses monoclonal antibodies which recognize an antigen of about 28-44 kDa of *T. equigenitalis,* and considers that such an antigen would correspond to the 52.7 (LPS) kDa protein recited in claim 18. This rejection is believed to be deficient.

The assertion in the Official Action that Akuzawa (1996) discloses monoclonal antibodies which recognize an antigen of 28-44 kDa of *T. equigenitailis* is a mere guess without legal basis. Based upon the cryptic description pieced together in the Official Action there is no way to determine whether Akuzawa (1996) describes monoclonal antibodies as claimed and/or whether the description in Akuzawa (1996) is an enabling disclosure of applicants' invention. To establish that the claimed monoclonal antibodies are inherently disclosed by Akuzawa (1996), the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. v. Monsanto Co.* , 948 F.2d 1264, 1268, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Id.* at 1269, 20 U.S.P.Q.2d at 1749 (quoting *In re Oelrich* , 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

Moreover, applicants believe that an antigen of about 22-44 kDa would not be considered as corresponding to the 52.7 (LPS) kDa protein recited in claim 17. There is no technical justification provided, and also no legal basis for concluding that the two are identical.

In addition, claim 16 recites monoclonal antibodies having a particular specificity. An anti-*T. equigenitalis* monoclonal antibody which lacks this specificity does not fall within the scope of claim 16 scope. Claims 17, 21 and 23 depend of claim 16, and claim 18 recites the same specificity as claim 16. The meager description in Akuzawa (1996) fails to disclose or even suggest that the monoclonal antibodies disclosed therein (if any) have the required specificity of the instant claims.

In view of the above, a prima facie case of unpatentability based upon this reference has not been made. Withdrawal of this rejection is respectfully requested and believed to be in order.

Claim 18 (17) has been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Friedrich (1995) in view of Sugimoto et al (1988). This rejection is respectfully traversed.

The failings of Friedrich (1995) with respect to applicants' claimed invention are provided *supra*. At the very least, Friedrich in no way discloses monoclonal antibodies having the specificity claimed by applicants. Nor does Sugimoto et al overcome or remedy this deficiency. Sugimoto et al describe outer membrane proteins of *Taylorella equigenitalis*. Contrary to the Examiner's allegations, Sugimoto el al do not teach or even

suggest any *T. equigenitalis* protein of 52.7, 120 or 150 (LPS) kDa. Figure 3 of Sugimoto et al does not show any such proteins. Nor are such proteins even suggested. Since Sugimoto el al does not describe or suggest any monoclonal antibody, and Friedrich (1995) does not disclose or suggest any *T. equigenitalis*-specific antibody, the combination of references fails to describe or even suggest the invention of claim 17.

Withdrawal of this rejection is respectfully requested and believed to be in order.

Claim 18 (17) has also been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Friedrich (1995) in view of Corbel et al (1982). This rejection is respectfully traversed.

As stated *supra*, Friedrich (1995) does not disclose or suggest any *T. equigenitalis*-specific antibody. The secondary reference, Corbel et al, describes antigens of *Haemophilis equigenitalis*. One of these antigens (page 535, paragraph 5) is assumed to be a polysaccharide, and, on this basis, is reported to have a molecular weight of about 1.8 x 10^5 Da. While Corbel et al may suggest the existence of a potential *H. equigenitalis* polysaccharide of about 180 kDa, it in no way discloses or even suggests a polysaccharide of about 18 kDa, as alleged in the Official Action.

Even if an 18 kDa *H. equigenitalis* polysaccharide were disclosed, this would still fail to render obvious the claimed invention in combination with Friedrich (1996). There is no basis, neither scientific nor legal, for considering an 18 kDa *H. equigenitalis* polysaccharide as teaching a 22 (LPS) kDa. The combination of Friedrich (1995) and Corbel el al thus fails to disclose or even suggest the claimed invention.

Claims 17, 19, 22, 24, 26, 28-29, 31, 35 and 37 (16, 18, 21, 23, 25, 27-28, 30, 34 and 36) have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Tainturier et al (1981) in view of Friedrich (1995) and Harlow: Antibodies, A Laboratory Manual (1988, chapters 4, 6, 9, 14 and 15). This rejection is respectfully traversed.

Tainturier et al teach that *H. equigenitalis* strains 001 and NCTC 11184 allow one to obtain rabbit antisera that strongly agglutinates the *H. equigenitalis* strains tested, and does not react with any of the other bacteria tested (see page 358, left column, "slide agglutination tests" and Table 3). However, Taintufier el al do not disclose or suggest *any* monoclonal antibody, much less a monoclonal antibody as instantly claimed. The disclosure relates only to antisera, i.e., to a composition which is a mixture of several products. There is, therefore, no disclosure of an isolated product which would recognize an epitope of a bacterium of the *T. equigenitalis* species, and which would not exhibit a crossed reaction with an epitope of a different *Taylorella* species, or of a non-*Taylorella* genus. The disclosure of Tainturier et al is thus devoid of relevance to the claimed invention.

As stated *supra*, Friedrich (1995) does not disclose or suggest any *T. equigenitalis*-specific antibody. Friedrich thus fails to overcome or remedy the deficiencies of Tainturier et al in disclosing or suggesting the claimed invention.

It is noted that with respect to the Harlow document, although five chapters were cited as apparently complete chapters, Applicants only received page 349 relating to "coupling antibodies to alkaline phosphatase", and pages 580-581 on "detecting and

quantitating antigens using the two-antibody sandwich assay". Sections 3 and 4 of page 580 were unreadable due to masking with an incident paper. The content of the Harlow chapters thus could not be studied by applicant and addressed herein. Should the Examiner maintain this rejection, a complete copy of the Harlow chapters cited by the Examiner is requested so that the rejection can be addressed in more detail.

Based upon the review of the pages received, it seems apparent that Harlow describes standard techniques which are in themselves not an object of the present invention. Harlow is unrelated to monoclonal antibodies having the specificity as instantly claimed. There is nothing in Harlow that would provide one skilled in the art with any motivation to obtain monoclonal antibodies having the specificity as instantly claimed. Harlow thus fails to overcome the deficiencies of Tainturier et al and Friedrich.

The combination of Friedrich, Harlow and Tainturier el al thus fails to disclose or even suggest applicants' claimed invention. Withdrawal of the rejection of the claims is thus respectfully requested and believed to be in order.

Claims 30, 33 and 34 (29, 32 and 33) have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Tainturier et al (1981) in view of Friedrich (1995) and Harlow, and further in view of Foster. This rejection is respectfully traversed.

The above comments regarding the combination of Tainturier et al (1981) in view of Friedrich (1995) and Harlow is incorporated by reference herein. In addition, Foster et al fails to overcome or remedy the deficiencies of the Tainturier et al (1981), Friedrich (1995) and Harlow combination.

The Foster et al patent discloses (1) immunoassays of total Ig in a biological fluid, (2) immunoassays of an allergen specific IgE in a biological fluid containing said IgE, and (3) an article for immobilizing reactants of an immunoreaction. Foster et al is unrelated to monoclonal antibodies as claimed in the instant invention. Foster et al is unrelated to monoclonal antibodies to *T. equigenitalis* generally as well as those having the claimed specificity. Foster et al thus fails to overcome or remedy the deficiencies of Tainturier et al, Friedrich and Harlow.

The combination of references cited in the Official Action thus fails to disclose or even suggest applicants' invention as claimed. Withdrawal of the rejection is respectfully requested and believed to be in order.

In view of the above, the claims of record are believed to be in condition for allowance. Further and favorable action in the form of a Notice of Allowance is respectfully requested and believed to be in order.

In the event that there are any questions relating to this amendment or the application in general, it would be appreciated if the Examiner would contact the undersigned attorney at the 508-339-3684 to expedite prosecution of this application.

Respectfully submitted,

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